Info on the 2017 Hormone Therapy Position Statement - NAMS

Changing the Conversation About Hormone Therapy

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Abstract and Introduction

Introduction

The 2017 Hormone Therapy Position Statement of The North American Menopause Society (NAMS)[1] allows the conversation about hormone therapy for menopausal women to be individualized for a specific woman. Instead of the recommendation of "lowest dose for the shortest period of time," the NAMS Hormone Therapy Position Statement Advisory Panel's review of the literature on hormone therapy suggests that women are better served using evidence-based information to determine the most appropriate type, dose, formulation, route of administration, and duration of use of hormone therapy. Decisions about hormone therapy should be based on the unique health risks of the woman, age or time from menopause, and goals of therapy.

The evidence suggests that, for menopausal women aged younger than 60 years or within 10 years of menopause onset, without contraindications, systemic hormone therapy benefits outweigh risks for relief of menopause hot flashes and sleep disturbances and for prevention of bone loss for those at elevated risk. This finding is in agreement with the 2016 Revised Global Consensus Statement on Menopausal Hormone Therapy.

When the initial results of the Women's Health Initiative (WHI) were released, there was widespread panic and concern among women taking hormone therapy and providers who prescribed it because of the risks identified for increased heart disease, breast cancer, venous thromboembolic events (VTE) and stroke, and dementia. However, in the 15 years since the initial results were released, additional results and analysis of the WHI have occurred, with publication of longer-term follow-up of up to 13 years as well as newer randomized trials and observational data.

The 23 national and international experts who served on the Advisory Panel reviewed all the key published data on hormone therapy for menopausal women. The review was not limited to one study, findings from one country, or one product. Data were reviewed on the effect of hormone therapy on cardiovascular disease (CVD) and diabetes; cancers, including breast, endometrial, lung, colon and ovary; osteoporosis and fracture prevention; mood and cognition; vasomotor symptoms (VMS); quality-of-life and economic issues; liver and gallbladder; musculoskeletal and joints; special senses (skin, eyes, ears); and genitourinary issues. Special populations evaluated included women with early menopause, whether natural, induced or surgical; those having BRCA genetic mutations with risk-reducing oophorectomy; and those who request extended duration because of persistent hot flashes, bone loss, or quality-of-life concerns. The Advisory Panel and the 2016–2017 NAMS Board of Trustees graded the level of evidence, provided key points, and identified areas of scientific uncertainty for which more research is needed before clear recommendations can be given.

The NAMS 2017 Hormone Therapy Position Statement is approximately 10,000 words long and published in July 2017. In addition to the comprehensive review and key points in each section, research priorities are identified, and clinical recommendations are provided at the end. NAMS hopes that this Hormone Therapy Position Statement will allow conversations about initiating, continuing, or stopping hormone therapy to be evidence-based, and not fear-based, and occur with a provider who is knowledgeable about all the available literature. The full Scientific Background Report for the Position

Statement is more than 40,000 words long and is available on the NAMS website (www.menopause.org/docs/2017-scientific-background).

The Position Statement Advisory Panel and the NAMS Board of Trustees recognize that the WHI is the largest and longest randomized, blinded trial ever performed, but the findings cannot be translated to women with early menopause initiating hormone therapy. The participants in the WHI were aged on average 63 years and were 13 years from menopause onset, and there was limited enrollment of women with bothersome VMS.

The WHI and the 13-year cumulative follow-up provide very important information about using standard-dose conjugated equine estrogen (CEE) combined with a potent synthetic progestin. However, for an individual woman, shared decision-making based on published reviewed literature should allow evaluation of unique health risks and goals of treatment and include potential benefits and risks from starting or continuing hormone therapy. The recent US Preventive Services Task Force draft evidence review, giving hormone therapy a D recommendation grade for prevention of chronic disease, misses the need for VMS relief in women with persistent bothersome symptoms, the efficacy of hormone therapy for prevention of osteoporosis and fracture, the improved quality of life seen by many women on hormone therapy, and the use of low-dose vaginal estrogen for treatment of genitourinary symptoms associated with estrogen loss.

There is "no one size fits all" when it comes to deciding about hormone therapy. There are many different types of hormone therapy formulations, with recognition that lower doses appear safer with fewer adverse events. In addition, the observational data showing fewer venous thromboembolic events (VTEs) and strokes with transdermal therapy provide options for women who wish to continue hormone therapy as they age. Women with a uterus who need protection against endometrial cancer if estrogen is being considered have options of micronized progesterone (shown in the E3N study to have less effect on breast cancer risk) and the new tissue-selective estrogen complex, CEE plus bazedoxifine, which is a progestogen-free combination protecting the uterus, providing relief of hot flashes and sleep disturbances, prevention of bone loss, and relief of vaginal symptoms without the adverse events of bleeding or breast tenderness seen with traditional estrogen/progestin combinations.

NAMS hopes that the recommendations from the Hormone Therapy Position Statement will remove fear from the conversation to allow shared decision-making on the basis of evidence-based information to determine what is best for a woman at any point in time. With longer duration of use, there is a need for continued evaluation and reassessment. Lowered doses or transdermal therapies may provide more benefits than risks for the individual woman.

Major Findings From the 2017 Hormone Therapy Position Statement of the North American Menopause Society

Hormone therapy is the most effective treatment for VMS and the genitourinary syndrome of menopause and has been shown to prevent bone loss and fracture.

The clearest benefit of hormone therapy is for the treatment of VMS and prevention of bone loss for those at elevated risk aged younger than 60 years or within 10 years of menopause onset, if there are no contraindications.

Age and time from menopause onset at initiation of hormone therapy are important determinants of the benefit-risk ratio.

In addition to a woman's health risks, risks of hormone therapy may differ for women depending on type, dose, duration, route of administration, and timing of initiation and whether a progestogen is needed.

Treatment should be individualized using the best available evidence to maximize benefits and minimize risks, with periodic re-evaluation about benefits and risks of continuing or discontinuing hormone therapy.

Compounded hormone therapies, despite celebrity hype, lack safety and efficacy data, are not monitored or regulated by the government, and have unique risks associated with compounding itself, including concerns about sterility; impurities; overdosing or underdosing, which could increase cancer risk; and lack of a label providing warnings about potential risks.

For women who initiate hormone therapy aged older than 60 years, certainly aged older than 70 years, or those who are more than 10 or 20 years from menopause onset, the use of hormone therapy has a less favorable benefit-risk ratio because of greater absolute risks of heart disease, stroke, VTEs, and dementia as women age.

The effects of hormone therapy on coronary heart disease (CHD) may vary depending on when hormone therapy is initiated in relation to a woman's age and/or time since menopause onset, with data suggesting reduced risk of CHD in women who initiate hormone therapy aged younger than 60 years and/or within 10 years of menopause onset. However, for women who initiate hormone therapy more than 10 years or clearly by 20 years from menopause onset, risk of CHD appears increased.

A significant reduction in all-cause mortality has been found in meta-analysis for women who initiate hormone therapy aged younger than 60 years and/or within 10 years from menopause onset. However, no protective effect was found in women with initiation more than 10 years from menopause onset.

Clinical Scenarios

Extended use of Hormone Therapy

There is no evidence to support routine discontinuation of hormone therapy after age 65. Decisions about longer durations of therapy should be individualized and considered for indications such as persistent VMS or bone loss, with shared decision making, documentation, and periodic re-evaluation.

Longer duration of use appears more favorable for estrogen therapy than for estrogen-progestin therapy, based on the WHI randomized, controlled trials.

Risks can be minimized with use of lower doses of both estrogen and progestogens, transdermal therapies to avoid the hepatic first-pass effect, and the combination of CEE paired with the tissue-selective estrogen receptor modulator bazedoxifine, which provides endometrial protection without the need for a progestogen.

Women With Only Vaginal Symptoms

For bothersome vulvovaginal or urinary symptoms not relieved with over-the-counter therapies and without indications for use of systemic hormone therapy, low-dose vaginal estrogen therapy or other therapies (ospemifene or intravaginal dehydroepiandrosterone) are recommended and can be continued as long as indicated. There is minimal absorption of low-dose vaginal estrogen, with levels within normal postmenopausal levels. Based on 1-year safety studies, progestogen is not needed with low-dose vaginal estrogen.

Special Populations of Women

Early Menopause
For women with hypoestrogenism, primary ovarian insufficiency, or early menopause, whether natural, surgical, or induced and without contraindications, hormone therapy is recommended until at least the median age of menopause (52 y) because observational data suggest that benefits exceed the risks for effects on prevention of osteoporosis and fracture, CVD, cognition and mood concerns, genitourinary syndrome of menopause, sexual function, and Parkinson disease.

Family History of Breast Cancer
Observational studies suggest that use of hormone therapy does not further alter the risk for breast cancer in women with a family history of breast cancer, although family history should be assessed when counseling about hormone therapy

Women Who are BRCA-positive but Who Have not Had Breast Cancer
For women who are BRCA-positive who have undergone risk-reducing bilateral salpingoophorectomy, observational data suggest that systemic hormone therapy to the median age of menopause to decrease health risks associated with premature loss of estrogen does not increase breast cancer risk, with decisions considered on an individual basis.

Survivors of Endometrial and Breast Cancer With Bothersome Vasomotor Symptoms
For women with prior estrogen-sensitive cancers, the use of hormone therapy is usually not recommended. Tested and effective nonhormone or complementary therapies should be used. If unsuccessful and systemic estrogen is considered for persistent symptoms, decisions should be made for compelling reasons after detailed counseling and in conjunction with their oncologists.

Prior Early Stage Endometrial or Breast Cancer With Bothersome Genitourinary Symptoms
On the basis of limited observational data, there appears to be minimal to no demonstrated risk for recurrence of early stage endometrial or breast cancer using low-dose vaginal estrogen, unless on aromatase inhibitors, but decisions should be made in conjunction with an oncologist after failure of nonhormone options.

Potential Risks of Hormone Therapy
Potential risks for women aged younger than 60 years or within 10 years of menopause onset include the rare risk of breast cancer seen with combination estrogen-progestin therapy, endometrial hyperplasia or cancer if the estrogen effect is inadequately opposed, VTE, and biliary issues. Additional risks across ages include myocardial infarction, stroke, and dementia.

Summary
In the recently published 2017 Hormone Therapy Position Statement of The North American Menopause Society and guidelines on hormone therapy, NAMS reaffirms the safety and efficacy of hormone therapy for menopausal women with bothersome VMS or for those at high risk for bone loss, particularly for those aged younger than 60 years or within 10 years of menopause onset. NAMS encourages practitioners to find the appropriate type, dose, formulation, route of administration, and duration of hormone therapy, with individualized shared decision making on the basis of evidence-based information and the unique health risks of the individual woman and with ongoing surveillance and periodic reassessment.